Correction

CHEMISTRY

The authors note that on page E2428, right column, in the Acknowledgments section, lines 4-5, “We also thank the US Department of Energy for support of this research (Grant SC0010662)” should instead appear as “This research is supported by the US Department of Energy, Office of Basic Energy Sciences, Division of Materials Sciences and Engineering under Award ER46430.”
Sensing of molecules using quantum dynamics

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We design sensors where information is transferred between the sensing event and the actuator via quantum relaxation processes, through distances of a few nanometers. We thus explore the possibility of sensing using intrinsically quantum mechanical phenomena that are also at play in photobiology, bioenergetics, and information processing. Specifically, we analyze schemes for sensing based on charge transfer and polarization (electronic relaxation) processes. These devices can have surprising properties. Their sensitivity can increase with increasing separation between the sites of sensing (the receptor) and the actuator (often a solid-state substrate). This counterintuitive response and other quantum features give these devices favorable characteristics, such as enhanced sensitivity and selectivity. Using coherent phenomena at the core of molecular sensing presents technical challenges but also suggests appealing schemes for molecular sensing and information transfer in supramolecular structures.

\textbf{Significance}

We explore the viability of using intrinsically quantum phenomena for molecular sensing. We formulate a theory for coherent sensing by combining the full analytical description of electronic relaxation processes with mass diffusion and charge transport models. This theory produces molecular-scale design criteria for sensors with responses rooted in quantum mechanical coherence phenomena. For example, the sensitivity of the detector can increase with decreased coupling between the molecular binding sites and the sensor substrate. Exploiting quantum properties of the analyte and the sensing element (e.g., electronic affinity, polarizability, etc.) enables enhanced discrimination among multiple analytes.

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associated with defects in solids (17), electronic energy transfer (18, 19), etc.] promises broad applications, for example in sensors that consist of nano-FET arrays (20). The mechanisms discussed here are especially relevant to processes at the nanoscale, where coherent or partially coherent quantum relaxation is more easily achieved at room temperature, compared to microscale systems.

Results and Discussion

Two-State Model for Coherent Sensing. In this section, we discuss the basic physics behind sensing through coherent CR, using a simple two-state $|\alpha\rangle$ and $|\beta]\rangle$ model for the sensing system. The system Hamiltonian is as follows:

$$
\hat{H} = \begin{pmatrix}
0 & V_{ad} \\
V_{ad} & \Delta E_{ad}
\end{pmatrix},
$$

where $V_{ad} = \langle d|\hat{H}|\alpha\rangle$ and

$$
\Delta E_{ad} = E_{d} - E_{a},
$$

with $E_{d} = \langle d|\hat{H}|d\rangle$ and $E_{a} = \langle a|\hat{H}|a\rangle$. The stationary electronic state is $|\psi\rangle = c_{d}|d\rangle + c_{a}|a\rangle$, and the asymmetry parameter, $\Delta E_{ad}/V_{ad}$, controls the populations of the two electronic states:

$$
|c_{d}|^2 = \frac{1}{2} \left( 1 + \frac{\Delta E_{ad}}{\sqrt{\Delta E_{ad}^2 + 4|V_{ad}|^2}} \right),
$$

$$
|c_{a}|^2 = \frac{1}{2} \left( 1 - \frac{\Delta E_{ad}}{\sqrt{\Delta E_{ad}^2 + 4|V_{ad}|^2}} \right).
$$

Perturbation by analyte binding changes the properties of state $a$ (e.g., an electronic state localized at the analyze-binding site), and hence the coherent evolution between states $a$ and $d$ (e.g., a distinct electronic state whose population determines the output signal of the sensor). The perturbation can change $\Delta E_{ad}$ and $V_{ad}$. For example, assuming no charge polarization before analyte binding ($\Delta E_{ad}/V_{ad} = 0$) and $\Delta E_{ad} > 0$ after binding, the population $|c_{d}|^2 = \frac{1}{2}$ (midway between the initial condition $|c_{d}|^2 = \frac{1}{2}$ and the full-polarization limit $|c_{d}|^2 = 1$) occurs when $\Delta E_{ad} = 2|V_{ad}|$. Thus, the magnitude of the energy perturbation required to polarize the system decreases as $|V_{ad}|$ drops. That is, more weakly coupled systems are more sensitive to analyte perturbation. This trend is reversed when the unperturbed system is asymmetric to begin with, namely, when $|\Delta E_{ad}| >> 2|V_{ad}|$.

Describing sensing with a two-state model lacks two key ingredients: (i) the two localized states may be coupled to manifolds of receptor surface states; (ii) thermal fluctuations may break the assumption of coherent quantum dynamics. Next, we consider these issues and their implications for sensing. The analysis of these issues will allow us to formulate different sensing approaches (and to provide design constraints and guidelines for their realization) that range from the coherent to the incoherent response of the sensing system to an external stimulus. Two of the sensing schemes described here may be used to interpret the experiments of Fig. 2 (see below), and discrimination between the two will result in further experimental investigation. However, the broader aim of our study is to map out potentially useful molecular-sensing strategies that could be implemented and explored in experiments of the future.

Sensing via Coherent Electronic Relaxation. We first model sensing where the perturbing event produces a localized state of the sensing system, which then relaxes coherently to a nearly infinite manifold $L = \{ |\ell\rangle \}$ of one-electron substrate states (Fig. 3). For example, analyte binding produces an excess electron or hole localization (described by either $|\alpha\rangle$ or $|\beta]\rangle$), and the Rabi oscillation between these two states is damped by quantum relaxation to the $L$ manifold. This transient relaxation affects the current through the junction that consists of source, conductive channel in the substrate (Fig. 1), and drain. Note that the physical model specifies neither the localization properties nor the charge donor/acceptor character of $|\alpha\rangle$ and $|\beta]\rangle$ (which is set by the initial condition).

Two classes of sensors are considered here. In one kind, the analyte binding prepares the sensing system in the $d$ or $a$ state and thus initiates the quantum relaxation process. In the other case, an external stimulus other than the analyte binding (a control signal) prepares the system in the $d$ or $a$ state and thus gives rise to the relaxation, whereas the relaxation properties (as determined by the energy and coupling parameters in Eq. 4) depend on whether or not an analyte molecule is attached to the sensing component when the control signal is generated.

The effective electronic Hamiltonian used to model the evolution of the perturbed system is as follows:

$$
\hat{H} = \hat{H}_{0} + \hat{V},
$$

where

$$
\hat{H}_{0} = E_{d}|d\rangle\langle d| + E_{a}|a\rangle\langle a| + \sum_{l} E_{l}|l\rangle\langle l|,
$$

with $E_{l} = \langle l|\hat{H}|l\rangle$ and, neglecting the direct $a-l$ coupling,

$$
\hat{V} = V_{ad}|d\rangle\langle a| + V_{ad}|a\rangle\langle d| + \sum_{l} (V_{af}|l\rangle\langle d| + V_{df}|d\rangle\langle l|).
$$

At time $t$,

$$
|\psi(t)\rangle = c_{d}(t)|d\rangle + c_{a}(t)|a\rangle + \sum_{l} c_{l}(t)|l\rangle.
$$

The time evolution in Eq. 5 for the initial condition

$$
|\psi(0)\rangle = |d\rangle
$$

was obtained using standard approaches (2) (SI Appendix). Eq. 6 can be interpreted in different ways that allow one to apply the same model to different types of analyte interactions and/or sensor operation. These interpretations are as follows: (i) charge is captured at site $d$ when the analyzer binds to the receptor group (at $t = 0$), and this charge then relaxes to the $L$ manifold. (ii) The triggering event (analyte binding or incident radiation) excites an electron charge (Fig. 4) that is stably localized on the anchoring site for $t < 0$ to another state localized mainly on $d$, but with nonnegligible couplings to $|a\rangle$ and $|\ell\rangle$. Then, the charge relaxes to the $L$ manifold as prescribed by $H$. (Note that this excitation–relaxation process does not require the presence of excess electron charge. The process may involve the local redistribution of an electron charge in a state of higher energy, with larger couplings to other, differently localized electronic states.) Removal of the external perturbation restores the initial localized state. (iii) $\hat{V}$ is the perturbation caused by analyte binding. $|d\rangle$ is an occupied frontier spin-orbital in the neutral or charged system that, after analyte binding, is coupled to the other (virtual) orbitals corresponding to $\hat{H}_{0}$. (iv) In a more elaborate sensor, charge localization on $d$ may be induced by an external source (for example, a gate voltage applied through wiring to the substrate). The perturbation at site $d$ produced by analyte binding influences the following charge relaxation, thus modulating the current signal. If the system is neutral, the charge localization on $d$ and its relaxation correspond to different polarizations of the sensing system. In all
of these cases, the model describes charge initially prepared on $d$ that relaxes “irreversibly” (2) to the $L$ manifold. This relaxation influences the electrostatic potential in the conducting channel and therefore the FET current. Note that the model described by Eqs. 4-6 also holds if $|d|$ and $|l|$ are delocalized surface states, provided that the coupling scheme in Eq. 4e is satisfied.

For $|\psi(0)| = |d\rangle$, the time-dependent $L$ manifold population is (SI Appendix):

$$P_L(t) \equiv \sum_i |c_i(t)|^2 = 1 - |c_d(t)|^2 - |c_l(t)|^2$$

$$= 1 - \frac{4|V_{ad}|^2}{\varepsilon^2} e^{-\gamma t/2} \left\{ \sinh^2 \left( \frac{\mu t}{2\hbar} \right) + \sin^2 \left( \frac{\nu t}{2\hbar} \right) \right\}$$

$$- e^{-\gamma/2t} \left\{ 1 + \gamma t + 2\gamma \cos \theta \right\}$$

$$+ \left\{ \frac{[1 - \gamma t - 2\gamma \cos \theta] e^{-\gamma t} - \chi \sin \theta \sin \left( \frac{\mu t}{2\hbar} \right) e^{\gamma t} + \chi \cos \theta e^{\gamma t} }{4} \right\}.$$ [7]

In Eq. 7, the density of $L$ states ($\rho_L$) was assumed independent of energy, and

$$\Gamma_d = 2\pi \langle |V_{ad}|^2 \rangle_L \rho_L; \quad \Delta E_i = \sqrt{\Delta E^2_{ad} + 4|V_{ad}|^2};$$

$$\varepsilon^2 = \sqrt{[\Delta E^2_{ad} - \Gamma^2_0/4] + \Gamma^2_0 \Delta E^2_{ad}};$$

$$u = \sqrt{\frac{\varepsilon^2 + \Delta E^2_{ad} - \Gamma^2_0/4}{2}}; \quad v = \text{sgn}(\Delta E_{ad}) \sqrt{\frac{\varepsilon^2 - \Delta E^2_{ad} + \Gamma^2_0/4}{2}};$$

$$\Gamma_d = \frac{\Gamma_d}{2} + v; \quad \chi = \frac{\sqrt{\Delta E^2_{ad} + \Gamma^2_d/4}}{\varepsilon}; \quad \theta = \arctan \frac{-v \Delta E_{ad} + u \Gamma_d/2}{u \Delta E_{ad} + v \Gamma_d/2}.$$ [8]

Because $\Gamma_d/2 - |v| \geq 0$, Eq. 7 describes population flow to the continuum: $P_L(t) \rightarrow 1$ for $t \rightarrow \infty$ (SI Appendix, Fig. S8). We now focus on the properties, and especially on the timescales, of the CR relevant to practical applications of the model. A critical issue is to reconcile the timescale of $P_L$ evolution (which modifies the gate voltage) with feasible current measurement times in a device. The analysis below addresses this issue and allows us to formulate design criteria for possible implementations of the sensing mechanism proposed in this section.

Charging the $L$ manifold correlates with removing charge from the $a$-$d$ system, which occurs on timescales that range from $\tau = 2h/\Gamma_d$ to $\tau = 2h/(\Gamma_d - 2\gamma)$ (in Fig. 3, $\tau = \tau_0$ or $\tau_m$ depending on the initial state of the sensor. In the timescale considerations, $\nu$ is assumed positive to simplify the notation). $\nu$ depends on the asymmetry $\Delta E_{ad}$, and on $V_{ad}$ and $\Gamma_d$ (Fig. 3 and Eq. 8). When these three parameters are all of the order of a millielectronvolts, the electronic relaxation occurs on the picosecond timescale. The relaxation time can be increased by orders of magnitude by decreasing $\Gamma_d$ or by making $\nu \sim \Gamma_d$ (SI Appendix). The former approach leads to a millisecond relaxation timescale for $\Gamma_d/2 \approx 10^{-11}$ eV (e.g., see SI Appendix, Fig. S8; such a small $\Gamma_d$ value may be realized in sensor architectures with an insulating layer between the receptor and the substrate). This timescale enables ready current measurement, but coherent (or at least partially coherent) quantum-state relaxation on this millisecond timescale requires a solid-state receptor layer (in this case, defects or impurities at its surfaces may, for example, act as the $a$ and $d$ sites) and low enough temperatures. In general, the quantum coherence leading to Eq. 7 is lost on the millisecond timescale of Figs. 6 and 8 (see below). However, coherent state dynamics can survive for as long as microsecond or millisecond for spin excitations associated with defects in solids (21-23), which motivizes use of spin relaxation as the sensing process, as an alternative to the relaxation of the spatial distribution of the electronic charge considered here. While decoherence due to the electronic-nuclear coupling is not included in our model, the properties of the electronic states and of their perturbation are kept as general as possible. In any case, coherent electronic relaxation through the receptor is more easily obtained in nanodevices than in microelectronic devices, because of the smaller length and timescales that characterize CR in nanodevices.

We now explore the physical conditions needed to produce coherent CR through a solid-state receptor on the millisecond timescale. First, we investigate FET design constraints that are required to obtain $\Gamma_d/2 \approx 10^{-11}$ eV. Then, we explore the compatibility of these architectural constraints with the coherent sensing model proposed here.

We assume a semiconducting substrate density of states of $\sim$1 nm$^{-3}$ eV$^{-1}$ (24). For $10 \times 10 \times 10$ (in units of nanometers to micrometers) slabs, one obtains $\rho_L$ values in the range of $10^{-7}$ to $10^{-10}$ eV$^{-1}$. With $\Gamma_d/2 \approx 10^{-11}$ eV, the first Eq. 8 leads to $|V_{ad}| \approx 10^{-15}$ to $10^{-24}$ eV. Assuming that $|V_{ad}| \approx V_\beta \exp(-\beta z)$ with $\beta \approx 1.4$ Å$^{-1}$ and $V_\beta \approx \Delta E_{ad} \approx 1$ eV, a 25- to 40-Å-thick dielectric layer needs to be inserted between the receptor $d$ sites and the substrate $l$ to realize the desired $\Gamma_d$ value. Otherwise, because $\beta \approx 2.3$ Å$^{-1}$ in vacuum (25), one can insert a vacuum gap with $z$ ranging from 15 to 24 Å.

These design parameters (25- to 40-Å-thick insulator or 15- to 24-Å-thick vacuum gap between receptor and substrate) are compatible with the coherent sensing mechanism based on the Hamiltonian of Eq. 4 if the transition between $|d|$ and $|l|$ is dominated by tunneling, despite the weak coupling expected at large distances. In the weak coupling regime, assuming $|V_{ad}| \ll \Delta E_{ad}$ and the two-state approximation, the system is localized on one site (for example, $d$) and the charge distribution tail on the other site is (Eq. 3) $|V_{ad}|/\Delta E_{ad} \approx \exp(-\beta z)$. Hopping through the insulator competes with $d$-$l$ tunneling if the insulator thermal occupation probability is appreciable. This probability is $\sim g \exp(-\Delta E/k_BT)$, where $k_B$ is Boltzmann’s constant, $T$ is the temperature, $\Delta E$ is the effective injection energy, and $g$ is an average electronic state degeneracy. Tunneling dominates hopping when (see ref. 26 for discussion of the hopping–tunneling transition):

$$\exp(-\beta z) > g \exp(-\Delta E/k_BT) \Rightarrow \Delta E > k_BT/\beta(\beta + \ln g).$$ [9]

Eq. 9 produces injection energies in the range of 0.9–2.3 eV, with $g$ computed from the density of states, based on typical electronic effective masses and the slab sizes considered above.
The discussion above suggests that sensing through coherent electronic relaxation is accessible. The analysis provides the geometric and energetic constraints on sensor design that are needed to access a millisecond timescale with $\Gamma_d$ values as small as $10^{-11}$ eV. Indeed, these constraints can be relaxed because the decay constant has the general form $\Gamma_d/2 - |\nu|$ (Eq. 8). $\nu$ depends on $V_{ad}$ and $\Delta E_{ad}$, which also influence the sensitivity and time evolution of the system response to a triggering event. $V_{ad}$ can be set by the receptor thickness, whereas $\Delta E_{ad}$ depends on the electronegativity of the a and d sites of the receptor.

To complete our sensor model, we describe the effect of the quantum relaxation process on the FET current. The change in $P_t$ implies CR in the substrate (Fig. 3). We model the source-conductive channel-drain system with a bridge level of unperturbed energy $\epsilon_0$ that changes to the following:

$$\epsilon_1(t) = \epsilon_0 + \eta P_t(t-t_0), \quad \text{[10]}$$

in response to changes in $P_t$. [If the initial condition of Eq. 6 is set for $t = t_0$, $t$ needs to be replaced by $t-t_0$ in the expressions of all state probabilities. Then, $P_t(t_0) = 0$.] The effective interaction parameter $\eta$ depends on the system geometry. In fact, $\eta$ is proportional to the average inverse distance between the substrate and the conductive channel. The model describes a sensing event that starts at $t_0$ (in Eq. 7, $t_0 = 0$).

Eq. 10 can be used directly in the modeling of electron transport through solid-state protein junctions (27, 28) or redox junctions (29–32). The semiconductor’s band structure should be used for quantitative descriptions of conduction through typical FET bridges. In this context, CR at the receptor–substrate interface changes the surface state-induced band bending (33).

The current through a junction with symmetric bridge–lead contacts and one bridge level (Eq. 10) is described using the Landauer–Büttiker formalism (34, 35):

$$I(t;V) = \frac{e^2}{\pi h} \int_{-\gamma}^{+\gamma} \frac{d\epsilon}{\pi} \frac{f_s(\epsilon;V) - f_D(\epsilon;V)}{\sqrt{[\epsilon - \epsilon_1(t)]^2 + \Delta E_{ad}^2}} \quad \text{[11]}$$

Here, $V$ is the bias voltage, $f_j$ ($j = S, D$) is the Fermi–Dirac distribution of electrode $J$, and $\gamma$ is the molecule–electrode coupling.
strength that is assumed energy independent. For \( \eta > 0 \), \( e_1 \) increases with \( P_L \), thus decreasing the current for fixed bias. The sensing mechanism is valid irrespective of the conduction regime. To show this, we also consider the limit of incoherent transport via charge hopping, which is the opposite limit of coherent transport (Eq. 11). For a one-level bridge (SI Appendix, Fig. S12), the current is as follows (29, 36):

\[
I(t; V) = e \frac{k_{\text{OR}}^{D} - k_{\text{RO}}^{D}}{k_{\text{OR}}^{S} + k_{\text{RO}}^{S} + k_{\text{RO}}^{D} + k_{\text{OR}}^{D}}.
\]

[12]

Here, \( O \) and \( R \) denote the oxidized and reduced bridge, respectively; \( k_{\text{OR}}^{D} \) is the rate constant for electron injection from the bridge to the source; \( k_{\text{OR}}^{S} \) is the rate of back ET to \( S \), and \( k_{\text{RO}}^{D} \) and \( k_{\text{OR}}^{D} \) denote the ET rates at the \( D \) contact [see the \( t \) and \( V \) dependence of these rates (31) in SI Appendix].

Eqs. 11 and 12 were developed for steady-state currents, but they can also be used to describe time-dependent currents that result from the evolution of \( P_L \) if \( e_1 \) changes sufficiently slowly for the current to adjust adiabatically to the value of \( e_1(t) \). The requirement for this adiabatic response is \( \tau >> 1/\gamma \) (clearly, this condition is more easily satisfied for \( \gamma \) values typical of the coherent tunneling regime), that is, the timescale (1/\( \gamma \)) for substrate-electrode ET needs to be much shorter than the characteristic time (\( \tau \)) for the electronic relaxation to the substrate and the consequent change in the gate voltage. When this condition is satisfied, the model for sensing that consists of Eqs. 7 (\( P_L \)), 10 (\( e_1 \)), and 11 or 12 (\( I \)) produces signals as in Figs. 5 and 6 (signals on much shorter timescales are shown in SI Appendix). The influence of the triggering event on the current is similar in the Landauer–Büttiker and hopping models. The induced relative change in the current is larger for a hopping mechanism, but the absolute values of the current and its change are larger for coherent tunneling.

In Fig. 5, electronic charge transferred to the substrate surface changes the gate voltage, thus increasing \( e_1(t) \) and reducing the current. (Note that, depending on the localization properties of the \( d \) and \( \{l \} \) states, the CR produced by the electronic state relaxation from \( d \) to the \( L \) manifold may amount to a change in the substrate charge by a small fraction of an electron charge per sensed event.) The normalized current signal is \( (I - I_0)/I_0 \), where \( I_0 \) is the constant current before sensing. \( I \) has a larger deviation from \( I_0 \) for the smaller value of \( V_{\text{ad}} \) (that is, the signal increases with decreasing electronic coupling between the surfaces of the receptor, as may result from using a thicker sensing element). The timescale of the signal evolution can change by orders of magnitude depending on parameters such as \( \Gamma_d \) (Fig. 5A and D), but the qualitative properties of the signal remain. The temperature dependence of the current does not significantly influence the normalized signal (Fig. 5A and C). Coherence can be maintained on the timescale of Fig. 5D, unless high-frequency vibrations intervene to destroy the signal coherence. Fig. 5 shows the robustness of the sensing mechanism to a variety of physical conditions. The accessibility of such conditions in real devices needs, however, to be explored in future experiments.

In the case of Fig. 6, the electronic relaxation to the \( L \) manifold is induced by an external control mechanism or other transient phenomenon. The event of interest changes the properties of the electronic relaxation dynamics and hence of the signal produced. The electronic relaxation to the substrate is much faster than the analyte diffusion to the receptor. Therefore, each quantum relaxation process generally occurs while the sensing site is free or bound, leading to \( I_1(t) \) or \( I_2(t) \), respectively. The magnitude of the signal increases with \( V_{\text{ad}} \) for the parameter choices in Fig. 6. The influence of analyte binding on the receptor properties is modeled as a change in \( \Delta E_{\text{ad}} \). The signal sensitivity to this change depends on the value of \( V_{\text{ad}} \) with respect to the range of \( \Delta E_{\text{ad}} \) values sampled during sensing. In general, the thickness (which controls \( V_{\text{ad}} \)), the surface chemistry (which determines \( \Delta E_{\text{ad}} \)), and the rigidity of the receptor are key design parameters, as highlighted in the above analysis and further detailed in SI Appendix.

We conclude this section by considering the case where analyte binding prepares the system in an initial (quantum) state localized at the binding site \( a \):

\[
|\psi(0)\rangle = |a\rangle.
\]

[13]

As in the case of Eq. 6, Eq. 13 may be used to describe many physical situations. The time-dependent population of the \( L \) manifold is now (SI Appendix):

\[
P_L(t) \equiv \sum_I |C_I(t)|^2 = 1 - \left(1 + \chi^2 + 2\chi \cos \theta \right) e^{-\Gamma_d t} \left[1 - \frac{\chi}{2} \cos \left(\frac{2\chi}{2} t\right) - \chi^2 \sin \left(\frac{2\chi}{2} t\right)\right] + \frac{1}{4} \left\{1 + \chi^2 - 2\chi \cos \theta \right\} e^{\Gamma_d t} + \left(\frac{\chi^2}{2} \frac{V_{\text{ad}}}{\xi}\right) \left[\sin^2 \left(\frac{V}{2} t\right) + \sinh^2 \left(\frac{V}{2} t\right)\right] \left[\frac{V_{\text{ad}}}{\xi^2} \left(\cos \left(\frac{V}{2} t\right) - \cos \left(\frac{2V}{2} t\right)\right) + \frac{\chi^2}{2} \left(\cos \left(\frac{V}{2} t\right) - \cos \left(\frac{2V}{2} t\right)\right)\right] e^{-\frac{\Delta E_{\text{ad}}}{k_B T}}.
\]

[14]

Substituting Eq. 14 into Eq. 10 and using Eq. 11 or 12 yield signals such as those shown in Fig. 7.

In the time range shown in Fig. 7, the rate of current decrease for a given \( V_{\text{ad}} \) drops with increasing \( \Delta E_{\text{ad}} \). This behavior, which is the opposite of that shown in Fig. 5, arises because the excess charge now is localized initially at site \( a \), which is distal to the substrate, and the \( d-a \) Rabi oscillations required for relaxation to the \( L \) manifold of substrate states have a decreasing amplitude (as well as a decreasing average transition probability) as \( \Delta E_{\text{ad}} \) increases.

All of the above signals plateau to the values corresponding to \( P_L(t) = 1 \) or \( P_L(t) = 1 \) for sufficiently long observation times.
(e.g., see SI Appendix, Fig. S2). Hence, the signals in each figure differ by the rate of variation between the initial (before sensing) and final plateaus. This behavior was observed in the experiments of Fig. 2 at longer times. However, no quantum coherence is generally expected in these experiments, due to thermal fluctuations that are not included in the modeling of this section. The above model is now examined. In one case, none of the one-electron Hamiltonian is given by Eq. 4a with:

\[ H_0 = E_d |d\rangle \langle d| + E_a |a\rangle \langle a| + \sum_l E_l |l\rangle \langle l| + \sum_r E_r |r\rangle \langle r|, \quad [15a] \]

\[ \dot{V} = V_{ad} |a\rangle \langle d| + V_{ad} |a\rangle \langle d| + \sum_l (V_{ad} |l\rangle \langle d| + V_{ad} |d\rangle \langle l|) + \sum_r (V_{ad} |r\rangle \langle a| + V_{ad} |a\rangle \langle r|). \quad [15b] \]

Two sensing mechanisms based on this one-electron Hamiltonian model are now examined. In one case, none of the one-electron states in Eq. 15 is occupied by the system in the absence of analyte, i.e., \(|d\rangle, |a\rangle, \{l\}\), and \(|r\rangle\) are virtual states. Analyte binding places the system in the \(a\) (Eq. 13) or \(d\) (Eq. 6) state. At time \(t\),

\[ |\psi(t)\rangle = C_d(t) |d\rangle + C_a(t) |a\rangle + \sum_l C_l(t) |l\rangle + \sum_r C_r(t) |r\rangle. \quad [16] \]

The system state relaxes to \(L\) and \(R\) with a characteristic time \(\tau\) (SI Appendix), so that the final occupation of the \(L\) manifold, which appreciably influences the gate voltage, is:

\[ P_L(t, \tau) = \frac{1}{1 + \frac{1}{4V_{ad}} \cdot \frac{1}{1 + \frac{1}{4V_{ad}}} \cdot 1} \quad [17] \]
is defined similarly to $\varepsilon_V$, a $\Gamma = \text{or} \Gamma_\text{e}$ (namely, by application of the present sensing model) if $\Gamma > 0.15 \text{ ns}$, $\Gamma = \text{manifolds on switches}$ if its initial localization was at $t_0$ to obtain $18 = \Gamma_0$ to the initially localized on site $t = 8 \Gamma_1 = \text{or} \Gamma_{\text{e}} \Gamma_0$ and $\Gamma_2 = \text{or} \Gamma_{\text{e}} \Gamma_0$ and $\Gamma_{\text{e}} \Gamma_0$ to the receptor. This assumption is according to the sensed event. thermal fluctuations) before sensing, whereas this gap increases by $0.06 \text{ eV}$ due to the sensed event.

($\Gamma_a$ is defined similarly to $\Gamma_a$ in Eq. 8, with $a$ and $L$ replacing $d$ and $R$) for the initial condition in Eq. 13, or as follows:

$$P_L(t \gg \tau) = \frac{1 + \frac{\Gamma_{\text{e}}}{\Gamma}}{1 + \frac{\Gamma}{\Gamma_{\text{e}}}}$$

[18]

for the initial condition in Eq. 6. We assume that, in the system under study, $\tau$ is negligible compared with the timescale for analyte diffusion to the receptor. This assumption is appropriate for many detectors where the analyte is sensed on second-to-minute timescales. Then, the occupation probability of $L$ switches “instantaneously” from $P_L = 0$ (or $P_L = 0$) to the value in Eq. 17 (18) because of interaction with the analyte. This value depends on the system properties and is denoted $P_L(P_L)$.

In another variant of the sensing mechanism, Eq. 17 or 18 describes the equilibrium distribution of the polarizable charge in the absence of analyte. This charge may be a valence electron of the neutral system, or an excess charge previously injected in $a$ or $d$ by a control external perturbation. Memory of the past evolution of the system is incorporated in the population of the $L$ manifold before analyte binding. In fact, this population is described by Eq. 17 if the charge was initially localized at site $a$, or by Eq. 18 if its initial localization was at $d$. $P_L(P_L)$ is the unperturbed equilibrium value of $P_L$, $P_L$. The analyte changes the system properties (that is, at least one of the coupling parameters $V_{\text{ad}}, \Gamma_{\text{e}}$, and $\Gamma_a$), so that $P_L(P_L) \rightarrow P_L(P_L)$.

In both sensing mechanisms, integration of the sensing system modeled by Eq. 15 in a FET allows one to distinguish between external stimuli at the $a$ or $d$ sites, provided that the charge distribution in Eq. 17 or 18 is not erased by thermal fluctuations and/or “communication” between the $L$ and $R$ manifolds on the timescale of the measurement. In fact, when analyte binding causes displacement of charge initially localized on site $a$, decreasing $|V_{\text{ad}}|$ (i.e., thickening the receptor layer; Fig. 3) decreases charge storage in $L$ (Eq. 17). In contrast, if the analyte causes charge displacement from $d$, thickening the receptor increases the $L$ manifold population (Eq. 18). Thus, depending on the electronic properties of the system and on the localization of the external stimulus, changes of the current from the unperturbed stationary value may increase or decrease with increasing receptor thickness, as described by the dependence of the substrate surface state ($L$) population on the $d-a$ coupling in Eqs. 17 and 18, and shown in Figs. 8 and 9. Selective sensing in enabled by responses such as those illustrated in Figs. 8 A and B or 9 A and B (namely, by application of the present sensing model) if different analyte species produce different initial charge redistributions in the receptor, according to Eqs. 17 and 18. The FET output signals in these figures are obtained by combining the above model for CR induced by analyte binding with a model for the analyte diffusion to the exposed surface of the receptor.

We model diffusion of the analyte as a one-dimensional process that obeys Fick’s second law with boundary conditions of constant analyte concentration at a distance $y$ above the top of the receptor, where the $a$ sites are located. If diffusion begins at $t = t_0$, the joint probability that an analyte molecule reaches the sensing surface and interacts with any receptor site $a$ at time $t$ is:

$$p(y, t) = p_0 \text{erfc} \left( \frac{y}{2 \sqrt{D(t - t_0)}} \right).$$

[19]

$D$ is the diffusion coefficient and $p_0$ is the interaction (or binding) probability. In contrast to the model of the previous section, it is not necessary to have very small values of $\Gamma_a$ and $\Gamma_\text{e}$ to obtain current signals on a long timescale, since the timescale of the change in the current is determined by analyte diffusion. Hence, the model may also be applied to the MOCSERs if the timescale of molecular motion is longer than that of electronic relaxation, if the charge distribution in Eq. 17 or 18 is sufficiently stable with respect to molecular motion, and if the influence of the nuclear

![Fig. 6. Normalized current signal vs. time, for a sensing mechanism in which a control perturbation produces the time-dependent current $I(t)$ and the event subject to detection alters this current. Eq. 11 models the current. The model parameters are as follows: $t_0 = 0.15 \text{ ns}$, $T = 298 \text{ K}$, $e_V = 0.2 \text{ eV}$, $\lambda = 0.3 \text{ eV}$, $\Gamma_{\text{e}}/2 = 10^{-6} \text{ eV}$, $V_{\text{ad}} = 2 \times 10^{-5} \text{ eV}$ (black lines) or $V_{\text{ad}} = 0.02 \text{ eV}$ (cyan lines), and $\Delta E_{\text{ad}} = k_\text{B}T/2$ (that is, a donor–acceptor energy gap within thermal fluctuations) before sensing, whereas this gap increases by $0.06 \text{ eV}$ due to the sensed event.](image)

![Fig. 7. Normalized current signal vs. time, for $V = 1 \text{ V}$, using the model that consists of Eqs. 14, 10, and (A) 11 or (B) 12. A (8) is the analog of Fig. 5A (Fig. 5B) for the initial condition in Eq. 13. The model parameters, line styles, and colors are as in Fig. 5.](image)
motion on the charge distribution does not erase or exceed the CR produced by the sensed event.

To describe conduction through the FET junction, the energy of the bridge level is modeled as follows:

$$e_1(t) = e_0 + e \left\{ 1 - p(y,t) \right\} P^0_L + p(y,t) P^- L \right\},$$  \[20\]

when Eq. 17 is used. $\{ P^0_L, P^- L \}$ is replaced by $\{ P^0_L, P^- L \}$ in Eq. 20 when Eq. 18 is used. $P^0_L$ or $P^- L$ is zero for the sensing mechanism where the triggering event creates the charge distribution in Eq. 17 or 18.

The model for sensing on the timescale of analyte diffusion described in this section consists of Eqs. 19 (analyte diffusion), 17 or 18 (CR in the substrate, near the receptor, due to the analyte), and 11 (current). The cases $P^0_L = 0$ (first sensing mechanism) and $P^0_L \neq 0$ (second sensing mechanism) are considered in Figs. 8 and 9. As expected from Eqs. 17 and 18, the decrease in the current is more (less) pronounced with increasing $\Gamma_d$, if the external perturbation occurs at the $a$ ($d$) site (compare Fig. 9 A and B). For $P^0_L \neq 0$, the dependence of the signal on $\Gamma_d$ can be inverted, depending on the changes in $\Gamma_d$ and $\Gamma_a$ caused by the analyte.

We expect that the conditions for the applicability of the present model to MOCSERs (see above) are likely very difficult to achieve, because thermal fluctuations and the long-range coupling between the $L$ and $R$ manifolds in most such molecular sensors can erase the charge distribution described by Eqs. 17 and 18. However, if the conditions of validity for the present model are satisfied (e.g., in systems were nuclear fluctuations are not effective in erasing the electronic charge distribution of Eqs. 17 and 18; note, however, that the feasibility of this condition needs to be established experimentally), our theoretical analysis yields the chemical–physical underpinnings of signals such as those in Fig. 2. In this case, Fig. 2 can be directly compared with Fig. 8 or Fig. 9.

Decoherence between the $L$ and $R$ populations, which may arise when the direct $L$–$R$ couplings cannot be disregarded as in Eq. 15b, would erase the information on the localization of the external stimulus at the $a$ or $d$ site, but would allow for a different sensing mechanism, as shown in the next section.

### Sensing Based on Analyte Diffusion and Incoherent CR.

The couplings between $L$ and $R$ states were neglected above because they were assumed to be sufficiently small that they have a negligible effect on the timescale $\tau$ of coherent CR. (The $a$–$L$ and $d$–$R$ couplings are not included in the model, because the occupation probabilities of the $a$ and $d$ sites are neglected on the $\tau_{incoherent}$ timescale.) In contrast, these couplings may be nonnegligible and produce incoherent CR on a timescale $\tau_{incoherent} >> \tau$. We describe CR between $L$ and $R$ in terms of equilibration of ET between the two manifolds of states. This model may describe the experimental data in Fig. 2. In fact, in the underlying experiments, the receptor is a (flexible) molecular layer and the current signal is generated by analyte diffusion on a minute timescale.

Another assumption of the sensing model in this section is that analyte diffusion to the receptor occurs on a timescale

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**Fig. 8.** Normalized current signal vs. time for $V = 1$ V, with (A) $P_L^0 = 0$ or (B) $P_L^0 = 0$, and CR induced by the sensed event starting from the initial condition in (A) Eq. 13 and (B) Eq. 6. Eqs. 17, 19, 20, and 11 were used. We set $\rho_0 = 1, t_0 = 1$, and $y/(2\sqrt{D}) = 1$ in Eq. 19, hence arbitrary units (a.u.) for time (depending on the system); $e_0 = 0.2$ eV, $f = 0.1$ eV, $e_0 - e_f = 0.2$ eV, $T = 298$ K, $\lambda = 0.3$ eV. The $a$–$d$ coupling in the absence of analyte is $V_{ad} = 10^{-3}$ eV ($V_{ad} = 0.01$ eV) for the black (cyan) line and is doubled after binding, whereas $\Gamma_a = \Gamma_d = 5 \cdot 10^{-3}$ eV.

**Fig. 9.** Normalized current signal vs. time, using Eq. 13 and for $P_L^0 \neq 0$. $I_0(t)$ is the current in the absence of analyte. $I_a$ is obtained by using $\Gamma_a = \Gamma_d = 2 \cdot 10^{-3}$ eV and Eq. 20 with $p = 0$. Eqs. 17, 19, 20, and 11 are used. After analyte binding, $\Gamma_a$ and $\Gamma_d$ change in (A) $\Gamma_a = \Gamma_d = 5 \cdot 10^{-3}$ eV and (B) $\Gamma_a = \Gamma_d = 0.02$ eV. The other parameters and the color code are the same as in Fig. 8.
that is longer than $\tau_{\text{incoherent}}$. The binding of analyte to the $a$ sites perturbs the energy differences among the $L$ and $R$ states (hence, the $L-R$ free-energy difference), thus leading to CR (repolarization) and to a consequent change in the electrostatic potential field in the conductive channel.

Incoherent CR is described by the classical master equations:

$$\frac{d|C_i|^2}{dt} = -|C_i|^2 \sum_l k_{il} + \sum_l |C_i|^2 k_{ir}, \quad [21a]$$
$$\frac{d|C_i|^2}{dt} = -|C_i|^2 \sum_r k_{ir} + \sum_r |C_i|^2 k_{il}. \quad [21b]$$

In Eq. 21, $k_{il}$ ($k_{ir}$) is the rate constant for ET from $|r\rangle$ to $|l\rangle$ (from $|l\rangle$ to $|r\rangle$). In this simple model, we assume that the ET rates are described by Marcus nonadiabatic ET theory. For $t \geq \tau_{\text{incoherent}} >> \tau$, the quantum information encoded in the $L$ and $R$ populations for $t \sim \tau$ is lost. Assuming an average energy difference $\Delta E$ between $L$ and $R$ states, this simple model leads to the Boltzmann result (see SI Appendix for the definition of $\tau_{\text{incoherent}}$):

$$P_L(t >> \tau_{\text{incoherent}}) = \frac{1}{1 + \exp\left(-\frac{\Delta E}{k_B T}\right)}. \quad [22]$$

Analyte binding changes $\Delta E$ to $\Delta E'$, and thus alters $P_L(t >> \tau_{\text{incoherent}})$. Using an electrostatic model for $\Delta E$ and making a multipole expansion of the charge distribution on an analyte particle (e.g., TATP in ref. 7), one obtains the following:

$$\Delta E' = \Delta E + \frac{A_1}{\lambda} + \frac{A_2}{\lambda^2} + \cdots. \quad [23]$$

where $\lambda$ is an effective distance between the regions where the $L$ and $R$ populations are distributed. $\lambda$ is approximated by the average $a-d$ distance if $L$ and $R$ are manifolds of surface electronic states. After modeling $\lambda$, one may obtain time-dependent currents similar to those in Fig. 2 using Eq. 22 in combination with Eq. 19 for the analyte diffusion, Eq. 20 for an effective bridge energy level in the junction, and Eq. 11 or 12 (or a band model) for the conduction. The model predicts that the output current signal increases or decreases with increasing $\lambda$ (as in the experiments of Fig. 2), depending on the expansion coefficients in Eq. 23 and, especially, on the sign of $A_1$. More detailed applications of this incoherent model require estimates of $A_1$ and are beyond the scope of the present study. The models developed above are summarized in Table 1.

**Conclusions**

We have provided a theoretical framework and designed guidelines for molecular-sensing devices based fundamentally on quantum dynamical effects. The theory links different sensing mechanisms and establishes the limits for their applicability, depending on FET device architectures and material proper-
ties. The coherent charge relaxation models require the use of solid-state materials for their implementation. One of the possible applications is, for example, to insulated and suspended gate FET devices (37, 38) that may use a selective layer made of conducting polymer (37). Application of the proposed sensing mechanisms to the devices in refs. 37 and 38 would require assessing both (i) the degree of coherence attainable and (ii) the measurement timescales allowed by different types of receptors. In other classes of sensors, the perturbing event directly changes the conductivity of a film between source and drain (39–45), and thus only one manifold of surface states should be used to model these systems.

Polaron models (2, 46) may be used to describe the receptor–substrate system and the conductance through the FET junction in future extensions of this study. The quantum master equation (2) or the reduced hierarchy equations of motion approaches (47) could be used to develop a general treatment of the incoherent evolution of the system after analyte binding. Our study (i) offers an in-depth analysis of sensing based upon coherent quantum relaxation processes, including device design constraints; (ii) affords a clear framework for future research; (iii) fosters explicit links between chemical sensing and quantum information theory, thus paving the way to use coherent control techniques (21) for molecular sensing. However, the feasibility of the proposed mechanisms for chemical sensing in practical detectors needs and deserves to be further studied theoretically and to be explored experimentally, in light of the encouraging comparisons with the experimental data of Fig. 2.

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